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Fast Folding Mutants of the Tetrahymena Ribozyme

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To further dissect the folding mechanism of the Tetrahymena ribozyme, x-ray footprinting of a “fast-folding” mutant of the *Tetrahymena thermophila* group I intron, L5b, has been completed during the past year. The “fast-folding” mutations identified by Dr. Williamson and his laboratory are of particular interest in that while they are located within the P4-P6 domain, they profoundly influence the folding of the catalytic core of the ribozyme. Dr. Williamson’s group has characterized the temperature and urea dependence of the slow steps of folding of these mutants using their oligonucleotide-hybridization method, which probes the formation of helix P3 in the ribozyme. However, this approach is unable to probe the fast transitions that can be followed by synchrotron footprinting. The analysis of the L5b ribozyme reveals the important result that complete folding of the P4-P6 domain is not obligatory for the formation of tertiary contacts between P4-P6 and other parts of the ribozyme. In particular, the peripheral helices that ring the catalytic core form more quickly than P4-P6 in L5b. This result demonstrates that folding of the ribozyme is not strictly sequential.